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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/655,531	09/05/2003	Jose Remacle	035642-0103	5573

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FOLEY AND LARDNER LLP
SUITE 500
3000 K STREET NW
WASHINGTON, DC 20007

EXAMINER

STEELE, AMBER D

ART UNIT	PAPER NUMBER
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1639

DATE MAILED: 11/17/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/655,531

Applicant(s)

REMACLE ET AL.

Examiner

Amber D. Steele

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 21 August 2006 and 26 May 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-30 is/are pending in the application.
- 4a) Of the above claim(s) 10-30 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-9 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date 12/3/2003.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

1. Claims 1-30 are currently pending.

Claims 1-9 are currently under consideration.

Election/Restrictions

2. Applicant's election of Group I (claims 1-9) in the reply filed on May 26, 2006 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

3. Claims 10-30 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on May 26, 2006.

4. Applicant's election of dopamine receptor 1A as the species of capture probe, human as the species of what the capture probe is derived from, dopamine receptor 1A as the species of target nucleic acid, and fluorescent label as the species of label in the replies filed on May 26, 2006 and August 21, 2006 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Information Disclosure Statement

5. The information disclosure statement filed December 3, 2003 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein in regard to citation number A3 has not been considered.

Specification

6. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Please refer to pages 14, 18, and 21. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01. Applicant is also requested to review the specification for additional hyperlinks and make appropriate corrections.

7. The disclosure is objected to because of the following informalities: Tables 2 and 4 contain accession numbers from Genbank®, since accession numbers are constantly updated, altered, and/or retired, applicants are requested to review the accession numbers and make any changes necessary.

Appropriate correction is required.

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8. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 1-9 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant is directed to the Guidelines for the Examination of Patent Applications under the 35 USC 112, first paragraph "Written Description" requirement, Federal Register, Vol. 66, No. 4 pages 1099-1111, Friday January 5, 2001. This is a **written description** rejection.

Claim 1 is drawn to a method for analyzing activation pathways comprising (a) obtaining a nucleic acid from a biological sample, (b) contacting the nucleic acid with a microarray comprising capture probes (sense and/or antisense; claim 6) derived from the 5 major subfamilies of amine neurotransmitter receptors, and (c) analyzing a 2-D pattern of data from the microarray. The invention as claimed encompasses all known sense and antisense probes and all potential sense and antisense probes and therefore comprises a vast number of probes. The claimed invention states that the probes and biological samples must be contacted under

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conditions that allow hybridization of complementary strands. The claimed invention does not include any structural information regarding the sense or antisense probes. In addition, antisense is commonly known in the art as a nucleic acid sequence that interferes with protein expression (since a definition of antisense is not provided in the specification, this definition is being utilized). The production of antisense probes is difficult for various reasons including the necessity to choose antisense probes with weak or absent homology for other nucleic acids beside the target, perfect homology of the antisense probe does not guarantee full specificity, stability, and preferential action (e.g. ability to block protein expression) of some sequences over others. Please refer to Nicot and Pfaff Journal of Neuroscience methods 71: 45-53, 1997 (particularly pages 47-50). Therefore, one of skill in the art would not reasonably conclude that the applicants had possession of all potential probes (particularly antisense probes).

The Specification teaches the names and accession numbers for some amine neurotransmitter receptors (please refer to Tables 1-4). However, the specification does not teach a single specific probe (sense or antisense) for any of the amine neurotransmitter receptors. Furthermore, the specification does not teach how to produce antisense (e.g. able to block protein expression) probes to the five major subfamilies of amine neurotransmitter receptors. Moreover, the specification does not teach which sequences would be able to define the various subtypes from the other including closely related subtypes of receptors. Therefore, one skilled in the relevant art would not reasonably conclude that the Applicants had possession of the entire scope of the presently claimed invention.

See Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or

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she was *in possession of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See page 1116.).

With the exception of probes consisting of full-length sequences corresponding to the accession numbers in Tables 2 and 4 as disclosed by the specification, the skilled artisan cannot envision the method of claim 1 and particularly the antisense probes of present claim 6. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class wherein the specification provided only the bovine sequence.

11. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

12. Claims 1-9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claim 1 and the dependent claims thereof recite the phrase "5 major subfamilies of amine neurotransmitter receptors", which renders the claims vague and indefinite. The

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specification and the claims do not define the phrase so that one of skill in the art would not be reasonably apprised of the metes and bounds of the claimed invention.

B. The term sub-subtype in claim 3 is indefinite. The term is not defined in the specification and one of skill in the art would not be able to determine the scope of the term. For example, is a sub-subtype a mutation of a naturally occurring subtype receptor? Is a sub-subtype of the receptors currently known in the art or art sub-subtypes unknown, etc.?

C. The 16 subtypes of cholinergic receptors (see claim 3) are indefinite. The specification has failed to describe or define 16 subtypes of cholinergic receptors. Cholinergic receptors are described as muscarinic and nicotinic with the muscarinic receptors further being defined as M1, M2, M3, M4, and M5. However, 16 subtypes of cholinergic receptors are not readily defined. Therefore, the 16 subtypes of cholinergic receptors are indefinite.

D. The 14 subtypes of trace amine receptors (see claim 4) are indefinite. The trace amines are defined as tyramine, b-phenylethylamine, and tryptamine in the specification and the TA1 and TA2 receptor subtypes are described. However, 14 subtypes of trace amine receptors are not readily defined. Therefore, the 14 subtypes of trace amine receptors are indefinite.

E. Claim 3 recites the limitations "dopamine", "histamine", "serotonin", "adrenergic", and "cholinergic" in lines 3-4. There is insufficient antecedent basis for the limitations in the claim.

F. Claim 4 recites the limitations "octopamine" and "trace amines" in lines 2-3. There is insufficient antecedent basis for the limitations in the claim.

Claim Rejections - 35 USC § 102

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

14. Claims 1 and 5-9 are rejected under 35 U.S.C. 102(e) as being anticipated by Kodira et al. U.S. Patent 6,890,731 filed August 4, 2000.

For present claim 1, Kodira et al. teach GPCR (G-protein coupled receptor) arrays which are utilized in methods for the development of therapeutics comprising obtaining a sample, hybridizing the sample to a nucleic acid array, and analyzing the sample (please refer to columns 1-5). In addition, Kodira et al. teach the generic GPCR superfamily and provide specific examples including dopamine receptors, cholinergic receptors, muscarinic receptors, serotonin receptors, adrenergic receptors, aminergic receptors, acetylcholine receptors, adrenaline receptors, and melatonin receptors (please refer to columns 2-5, 23-33).

For present claim 5, Kodira et al. teach dopamine receptors 1-5, thirteen serotonin 5-HT receptors and serotonin 5-HT₃ receptor, three subtypes of adrenergic beta receptors, three subtypes of adrenergic alpha₁ receptors, and three subtypes of adrenergic beta₂ receptors (please refer to columns 2-5).

For present claim 6, Kodira et al. teach coding, noncoding, 5'-3', 3'-5', and antisense probes (please refer to columns 23-26 and 31).

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For present claim 7, Kodira et al. teach RNA and cDNA (please refer to columns 23 and 31).

For present claim 8, Kodira et al. teach labeling nucleic acid (please refer to column 31).

For present claim 9, Kodira et al. teach fluorescent labels (please refer to column 31).

Therefore, the presently claimed invention is anticipated by the teachings of Kodira et al.

15. Claims 1, 3, and 5-9 are rejected under 35 U.S.C. 102(e) as being anticipated by Williams et al. U.S. Patent 6,964,868 filed January 28, 1999.

For present claim 1, Williams et al. teach methods utilizing 7 transmembrane receptors of the rhodopsin family and G-protein coupled receptors comprising providing a sample, hybridization of the sample with an array, and identifying differentially expressed genes or proteins in the sample (please refer to columns 2-5, 12-19, 23-38; Example 3).

For present claims 3 and 5, Williams et al. teach serotonin 5-hydroxytryptamine 1A-1F, 2A-2C, 4, 5A-5B, 6, and 7 (14 serotonin receptors); acetylcholine receptor (1 cholinergic receptor); muscarinic receptors M1-M5 (5 additional cholinergic receptors); adenosine receptors; adrenergic alpha-1A-1C, alpha-2A-2D, beta-1-3 (10 adrenergic receptors); angiotensin II receptors; bradykinin receptors; cannabinoid receptors; dopamine receptors D1-D5 (5 dopamine receptors); histamine H1 and H2 receptors (2 histamine receptors); octopamine receptor (1 octopamine); tryptamine receptor (1 trace amine); opioid receptors (please refer to Example 3).

For present claim 6, Williams et al. teach coding, noncoding, and antisense probes (please refer to abstract; columns 12-19, 28).

For present claim 7, Williams et al. teach RNA and cDNA (please refer to columns 7-8, 25).

For present claim 8, Williams et al. teach labeling nucleic acids (please refer to columns 7, 25-26, 32-33).

For present claim 9, Williams et al. teach fluorescent labels (please refer to columns 7, 25-26, 32-33).

Therefore, the presently claimed invention is anticipated by the teachings of Williams et al.

Claim Rejections - 35 USC § 103

16. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

17. Claims 1-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kodira et al. U.S. Patent 6,890,731 filed August 4, 2000; Borowsky et al. PNAS 98(16): 8966-8971, 2001 (June 31); Oda et al. Folia Pharmacol. Jpn. 118: 36-42, 2001 (July); Hosey The FASEB Journal 6: 845-852, 1992; and Dani Biol. Psychiatry 49: 166-174, 2001.

For present claim 1, Kodira et al. teach GPCR (G-protein coupled receptor) arrays which are utilized in methods for the development of therapeutics comprising obtaining a sample, hybridizing the sample to a nucleic acid array, and analyzing the sample (please refer to columns 1-5). In addition, Kodira et al. teach the generic GPCR superfamily and provide specific

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examples including dopamine receptors, cholinergic receptors, muscarinic receptors, serotonin receptors, adrenergic receptors, aminergic receptors, acetylcholine receptors, adrenaline receptors, and melatonin receptors (please refer to columns 2-5, 23-33).

For present claims 3 and 5, Kodira et al. teach dopamine receptors 1-5 (5 dopamine receptors), thirteen serotonin 5-HT receptors and serotonin 5-HT₃ receptor (14 serotonin receptors), three subtypes of adrenergic beta receptors, three subtypes of adrenergic alpha receptors, and three subtypes of adrenergic beta₂ receptors for a total of 9 adrenergic receptors (please refer to columns 2-5).

For present claim 6, Kodira et al. teach coding, noncoding, 5'-3', 3'-5', and antisense probes (please refer to columns 23-26 and 31).

For present claim 7, Kodira et al. teach RNA and cDNA (please refer to columns 23 and 31).

For present claim 8, Kodira et al. teach labeling nucleic acid (please refer to column 31).

For present claim 9, Kodira et al. teach fluorescent labels (please refer to column 31).

However, Kodira et al. do not specifically teach 2 or 4 subtypes of histamine receptors. In addition, Kodira et al. do not specifically teach 4 or 16 subtypes of cholinergic receptors. Furthermore, Kodira et al. do not specifically teach 1 subtype of octopamine or 14 subtypes of trace amines.

For present claims 3 and 5, Oda et al. teach histamine receptors H₁, H₂, H₃, and H₄ are GPCRs (e.g. two histamine receptors; please refer to abstract English translation on page 42; Tables 1-2; Figures 1-2).

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For present claims 3 and 5, Dani teaches nicotinic receptors are part of the acetylcholine receptor family and comprise $\alpha 1$ - $\alpha 9$, $\beta 1$ - $\beta 4$, δ , ϵ , and γ wherein the α and β subunits form various $\alpha\beta$ combinations (e.g. at least 16 cholinergic receptor subtypes; please refer to abstract; Introduction; Multiple Subunits Produce Nicotinic Receptor Diversity).

For present claims 3 and 5, Hosey teaches both muscarinic and nicotinic members of the cholinergic receptor family including $\alpha 2\beta\gamma\delta$, $\alpha 2\beta\delta\epsilon$, $\alpha 2\beta 3$, and M1-M5 (e.g. at least 8 cholinergic receptor subtypes; please refer to abstract; pages 845-846).

For present claims 4-5, Borowsky et al. teach 15 G-protein coupled receptors including TA1 and TA2, one orphan receptor PNR, and octopamine that are receptors for trace amines (please refer to abstract; Introduction; Figures 1 and 3-4; Table 1; Results; Discussion).

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to alter the methods for the development of therapeutics utilizing arrays comprising GPCRs, dopamine receptors, cholinergic receptors, muscarinic receptors, serotonin receptors, adrenergic receptors, aminergic receptors, and acetylcholine receptors taught by Kodira et al. with the specific receptors taught by Oda et al., Dani, Hosey, and Borowsky et al.

One having ordinary skill in the art would have been motivated to do this because Kodira et al. teach GPCRs including amine neurotransmitter receptors comprising the cholinergic receptor family, the dopamine receptor family, the serotonin receptor family, and the adrenergic receptor family. While Kodira et al. specifically teaches some members of the genus (e.g. dopamine receptors 1-5, thirteen serotonin 5-HT receptors and serotonin 5-HT₃ receptor, three subtypes of adrenergic beta receptors, three subtypes of adrenergic alpha₁ receptors, and three subtypes of adrenergic beta₂ receptors), Kodira et al. does not teach specifically list all of the

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species of the genus. However, the members of the amine neurotransmitter receptor family are known in the art (e.g. 5 receptor subtypes for dopamine, 4 receptor subtypes for histamine, 14 receptor subtypes for serotonin, 5 subtypes for adrenergic receptors, 16 subtypes for cholinergic receptors, octopamine, and 14 subtypes of trace amine receptors; please refer to Oda et al., Dani, Hosey, and Borowsky et al.). In addition, Kodira et al. teach that various GPCRs are important in various diseases including Parkinson's disease, depression, schizophrenia, Tourette's syndrome, tardive dyskinesia, Huntington's disease, OCD, panic disorder, anxiety disorder, social phobia, migraines, side effects of chemotherapy, and gastric motility disorders and thus are useful in screening for drug targets (please refer to columns 1-5 and 12). Furthermore, the addition of all known dopamine receptors, histamine receptors, serotonin receptors, adrenergic receptors, cholinergic receptors, and trace amine receptors in the array utilized in the method would be a design choice based on the desired outcome of the screening method.

One of ordinary skill in the art would have had a reasonable expectation of success in the modification of methods for the development of therapeutics utilizing arrays comprising GPCRs, dopamine receptors, cholinergic receptors, muscarinic receptors, serotonin receptors, adrenergic receptors, aminergic receptors, and acetylcholine receptors taught by Kodira et al. with the specific receptors taught by Oda et al., Dani, Hosey, and Borowsky et al. because of the various references provided and incorporated by reference by Kodira et al. regarding how to prepare microarrays (please refer to columns 30-33).

18. Claims 1-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Williams et al. U.S. Patent 6,964,868 filed January 28, 1999; Borowsky et al. PNAS 98(16): 8966-8971, 2001

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(June 31); Oda et al. *Folia Pharmacol. Jpn.* 118: 36-42, 2001 (July); and *Dani Biol. Psychiatry* 49: 166-174, 2001.

For present claim 1, Williams et al. teach methods utilizing 7 transmembrane receptors of the rhodopsin family and G-protein coupled receptors comprising providing a sample, hybridization of the sample with an array, and identifying differentially expressed genes or proteins in the sample (please refer to columns 2-5, 12-19, 23-38; Example 3).

For present claims 3-5, Williams et al. teach serotonin 5-hydroxytryptamine 1A-1F, 2A-2C, 4, 5A-5B, 6, and 7 (14 serotonin receptors); acetylcholine receptor (1 cholinergic receptor); muscarinic receptors M1-M5 (5 additional cholinergic receptors); adenosine receptors; adrenergic alpha-1A-1C, alpha-2A-2D, beta-1-3 (10 adrenergic receptors); angiotensin II receptors; bradykinin receptors; cannabinoid receptors; dopamine receptors D1-D5 (5 dopamine receptors); histamine H1 and H2 receptors (2 histamine receptors); octopamine receptor (1 octopamine); tryptamine receptor (1 trace amine); opioid receptors (please refer to Example 3).

For present claim 6, Williams et al. teach coding, noncoding, and antisense probes (please refer to abstract; columns 12-19, 28).

For present claim 7, Williams et al. teach RNA and cDNA (please refer to columns 7-8, 25).

For present claim 8, Williams et al. teach labeling nucleic acids (please refer to columns 7, 25-26, 32-33).

For present claim 9, Williams et al. teach fluorescent labels (please refer to columns 7, 25-26, 32-33).

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However, Williams does not specifically teach 4 subtypes of histamine receptors. In addition, Williams does not specifically teach 16 subtypes of cholinergic receptors. Furthermore, Williams does not specifically teach 14 subtypes of trace amines.

For present claims 3 and 5, Oda et al. teach histamine receptors H1, H2, H3, and H4 are GPCRs (e.g. two histamine receptors; please refer to abstract English translation on page 42; Tables 1-2; Figures 1-2).

For present claims 3 and 5, Dani teaches nicotinic receptors are part of the acetylcholine receptor family and comprise $\alpha 1$ - $\alpha 9$, $\beta 1$ - $\beta 4$, δ , ϵ , and γ wherein the α and β subunits form various $\alpha\beta$ combinations (e.g. at least 16 receptor subtypes; please refer to abstract; Introduction; Multiple Subunits Produce Nicotinic Receptor Diversity).

For present claims 4-5, Borowsky et al. teach 15 G-protein coupled receptors including TA1 and TA2 and one orphan receptor PNR that are receptors for trace amines (please refer to abstract; Introduction; Figures 1 and 3-4; Table 1; Results; Discussion).

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to modify the method utilizing receptors of the rhodopsin family and G-protein coupled receptors including 14 serotonin receptors; acetylcholine receptor; muscarinic receptors M1-M5; adrenergic $\alpha 1$ A-1C, $\alpha 2$ A-2D, $\beta 1$ -3 receptors; dopamine receptors D1-D5; histamine H1 and H2 receptors; octopamine receptor; and tryptamine (trace amine) receptor on an array to identify differentially expressed proteins and/or nucleic acids with the specific receptors taught by Oda et al., Dani, and Borowsky et al.

One having ordinary skill in the art would have been motivated to do this because Williams et al. teaches the genres of GPCR, rhodopsin family receptors, serotonin receptors,

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acetylcholine receptors, muscarinic receptors, adrenergic receptors, cholinergic receptors, dopamine receptors, histamine receptors, octopamine receptor, and tryptamine receptor. While all the known species of the various genres were not specifically taught by Williams et al., 5 receptor subtypes for dopamine, 4 receptor subtypes for histamine, 14 receptor subtypes for serotonin, 5 subtypes for adrenergic receptors, 16 subtypes for cholinergic receptors, octopamine, and 14 subtypes of trace amine receptors are known in the art (please refer to Oda et al., Dani, Hosey, and Borowsky et al.). In addition, Williams et al. teach that the rhodopsin family and GPCRs can be utilized for chromosome mapping, tissue profiling including in cancer cells, diagnosis or prognosis of diseases, determining differential expression of proteins and/or nucleic acids (please refer to columns 25-31). Furthermore, the addition of all known dopamine receptors, histamine receptors, serotonin receptors, adrenergic receptors, cholinergic receptors, and trace amine receptors in the array utilized in the method would be a design choice based on the desired outcome of the screening method.

One of ordinary skill in the art would have had a reasonable expectation of success in the modification of the method utilizing receptors of the rhodopsin family and G-protein coupled receptors including 14 serotonin receptors; acetylcholine receptor; muscarinic receptors M1-M5; adrenergic alpha-1A-1C, alpha-2A-2D, beta-1-3 receptors; dopamine receptors D1-D5; histamine H1 and H2 receptors; octopamine receptor; and tryptamine (trace amine) receptor on an array to identify differentially expressed proteins and/or nucleic acids with the specific receptors taught by Oda et al., Dani, and Borowsky et al. because of the various literature provided by Williams for producing microarrays (please refer to column 28).

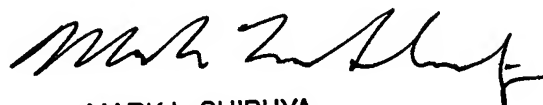
Future Communications

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amber D. Steele whose telephone number is 571-272-5538. The examiner can normally be reached on Monday through Friday 9:00AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

ADS
November 1, 2006



MARK L. SHIBUYA
PRIMARY EXAMINER